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Bacteremia in Subjects with Sickle Cell Disease: High Rate of Gram-Negative Isolates in the West African Context

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Abstract

Background: Sickle cell disease is one of the most common monogenic diseases in the world, affecting approximately 70 million people, 80% in sub-Saharan Africa and 1 in 10 in Senegal. Sickle cell anemia causes functional asplenia (associated with repeated thrombosis of splenic vessels), resulting in increased susceptibility to infection. However, several studies have reported differences in the spectrum of bacterial infections in malaria-endemic areas. Therefore, we proposed to conduct a study to determine the rate of positive blood cultures and the bacteriological spectrum in sickle cell patients. **Materials and Method:** This is a descriptive cross-sectional study of blood culture samples from patients who received a request for hemoglobin electrophoresis as part of their treatment at the Principal's hospital in Dakar. The study took place from January 2008 to December 2021. For each patient, we collect demographic information, including age, gender, and the service from which the analysis request originated. Data were collected in the laboratory's computer system and entered into Microsoft Excel (2007). Statistical analyzes were performed using Epi-Info 7 software. **Results:** Our study included 1419 patients. The most common types of hemoglobin profiles were: normal profile (n = 1025), AS profile (n = 283), SS profile (n = 104), SC profile (n = 7). This corresponds to the proportions of 72%, 20%, 0.5% and 7.5% for the profiles Normal, AS, SC and SS. The male proportion was 61.1%, 61.5%, 57.1, respectively %,

55.8% for Normal, SA, SC, and SS profiles. A total of 19,090 individual blood culture bottles were collected from 1419 impatient patients as follows: Normal profile (n = 18,042 bottles), AS profile (n = 677 culture bottles), SS profile (n = 362 bottles). The majority of blood culture orders come from pediatric services, accounting for 70% of the total number of orders. Of 19,090 vials examined in this current study, 19.6% developed a positive blood culture. Overall, the most commonly isolated bacteria were Staphylococci (41.1%), Enterobacteriaceae (36.7%), Bacillaceae (10.2%), unfermented (6.30%), Streptococci (5.01%), and a small proportion of yeast (0.75%). There is no significant difference in bacterial spectrum between the SS profile and the normal profile of individuals (p = 0.104). Coagulase-negative staphylococci accounted for 32%, 24%, and 40% of the species isolated in the normal AS and SS profiles. respectively. Coagulase-negative staphylococci were the most commonly isolated organisms in SS. Group E and sp-tagged streptococci each account for less than 2% of the organisms isolated in SS. Pneumococci were not found. *Bacillus* accounts for 25% of isolates in SS subjects compared to 9% in normal and AS subjects, respectively. *Pseudomonas aeruginosa* and *Burkholderia cepacia* then make up 10% of the isolates in the subjects of the SS profile as non-fermenters. **Conclusion:** Our study shows that enterobacteria and staph are prevalent in people with sickle cell disease. There is no significant difference in bacterial spectrum between SS subjects compared to subjects with a normal profile. The rarity of *Streptococcus pneumoniae* in bacteremia isolates underlines the need for further studies with larger patient numbers to better understand the spectrum of bacterial infections in patients with sickle cell disease in West Africa.

Keywords

Sickle Cell Disease, Senegal, Bacteremia, Blood Culture, Infection

1. Introduction

Sickle cell anemia is one of the most common monogenic diseases in the world, affecting approximately 70 million people, 80% of whom live in sub-Saharan Africa [1] [2] [3]. In Senegal, one in ten people carries the sickle cell gene [4] [5], regardless of their ethnic, geographical or social origin. Sickle cell disease causes functional asplenia (associated with iterative thrombosis of splenic vessels) [6]. In sickle cell S/S or S/0, asplenia is common and effective from six to 12 months of age, while in S/thalassemia it is more fortunate and less frequent at later ages [6] [7]. In addition, there is intestinal necrosis associated with filling of small vessels by sickle cells, resulting in injuries with translocation of digestive bacteria into the blood system and congestion in the vessels causing infection [8] [9]. Recent studies have reported a possible modulation of antibacterial activity in sickle cell carriers carrying mutations in the IGF1R (insulin growth factor 1 receptor) and TGF/BMP genes. This leads to increased sensitivity to bacterial agents

[10]. People with sickle cell anemia are therefore at higher risk of serious bacterial infections: bacteremia, meningitis, osteomyelitis, pneumonitis [9] [11]. The risk is increased for encapsulated bacteria: *Streptococcus pneumoniae*, *Haemophilus influenzae*, Group B *Streptococcus*, *Neisseria meningitidis*. Intracellular germs can also be found. Bone infarction predisposes to osteomyelitis, particularly Salmonella and Escherichia coli (*E. coli*). The latter is also involved in pyelonephritis. Mandatory vaccination against *Haemophilus influenzae* has virtually eradicated this bacterium, to which patients with sickle cell anemia are very sensitive. *Streptococcus pneumoniae* is the most common cause of bacteremia in sickle cell anemia, particularly in children under the age of three [12]. However, several studies have reported differences in the spectrum of bacterial causes of bacteremia in malarial areas [13]. This difference in bacterial spectrum can impair the effectiveness of prophylaxis [14] [15]. In Senegal, data on the spectrum of isolated bacteria is not always available, especially in the periphery where blood culture instruments are not always available. It is important to feed the local bacterial spectrum database to better manage sickle cell infections. Limited data are also available for heterozygous bacteremia, which is also common in tropical areas. Therefore, we proposed to conduct this study to determine the rate of positive blood cultures in sickle cell patients. Second, to describe the spectrum of bacteria involved in sepsis in sickle cell patients. These results will help to better understand the treatment of sickle cell disease in both curative and preventive ways.

2. Method

2.1. Study Area Description

The Hospital Principal is located in Dakar, the capital of Senegal, in the extreme west of the Cape Verde peninsula, on the edge of the Atlantic Ocean. Like the rest of the country, Dakar has a tropical climate. It covers an area of 83.7 km^2 and has an estimated population of 3,835,019 (**Figure 1**).

Figure 1. The Dakar hopital principal (HPD).

2.2. Study Design

This is a descriptive cross-sectional study of blood culture samples from sickle cell patients. The study took place from January 2008 to December 2019. Demographic data were collected for each patient, namely age, sex, service that requested the biological analysis. For each patient, samples were collected in an anticoagulant tube (EDTA) for a hemoglobin electrophoresis study at alkaline pH (8.8) and secondary pH (5.4). Hemoglobin fractions were quantified using the Hydrasis Sebia densitometer (ref.). A total of 1 mL blood sample was collected from a fresh venous puncture site and placed in a vial containing 10 mL blood agar culture medium. Blood cultures were incubated aerobically at 37˚C and observed for three consecutive days to obtain preliminary results by verifying the presence of hemolysis, air bubbles (gas generation) and coagulation of the broth on the culture medium. When the incubation is completed with Bactec automate, the positive bottles will be displayed by the machine. This was followed by a microscopic examination in the fresh state and after Gram staining. The positive vials were cultured in Mueller Hinton medium or enrichment medium. The galleries allowed identification of bacteria that had evolved. The blood culture was only reported negative after 10 days of observation.

2.3. Data Collection and Analysis

Viral load age and sex information was collected for all patients via the laboratory's computer system. Data entry and statistical analysis were performed with Epi-info version 7. Mean values and their standard deviations as well as medians and their interquartile ranges (IQR) were calculated for the quantitative variables. The proportions of qualitative variables were determined with a confidence interval (CI) of 95%. Outcome variables were viral load status. Cross-tabulations were created from the result variables and the socio-demographic variables (age, gender). Chi-square or Fisher's exact test was used as a statistical significance test to compare sociodemographic variables with viral load status. A p-value < 0.05 from two-tailed tests was considered significant in all tests. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to determine associations between sociodemographic variables and viral load status.

2.4. Ethical Consideration

To ensure privacy, survey data is collected using password-protected laboratory software and compiled. The results of the study will shed light on the spectrum of bacterial infections in sickle cell populations. The results will second help guide the best decisions and strategies to prevent and treat infections in sickle cell populations.

3. Results

3.1. Study Population

Our study included 1419 patients. The most common types of hemoglobin pro-

files were: normal profile (n = 1025), AS profile (n = 283), SS profile (n = 104), SC profile (n = 7). This corresponds to the respective proportions of 72%, 20%, 0.5% and 7.5% for the Normal, AS, SC and SS profiles. The male sex ratio dominance was 61.1% and 61.5% for the observed Normal and SA profiles, compared to 57.1% and 55.8% for SC and SS profiles (Table 1).

3.2. Blood Culture

3.2.1. Blood Culture Provenance

A total of 19,090 individual blood culture bottles were collected from 1419 impatient patients as follows: normal profile (n = 18,042 bottles), AS profile (n = 677 culture bottles), SS profile (n = 362 bottles). The majority of blood culture orders is from pediatric services (70%) and account for 70% of the total number of prescriptions. Thus, 70%, 61% and 53.6% of the prescriptions made in normal profiles, AS and SS originate from pediatrics. Children under the age of 1 account for 54% of prescriptions issued. 67% of prescriptions issued in the SS are for patients under 10 years of age. The age range of 1 to 5 years includes the majority of hemoculture prescriptions in SS, accounting for 37% of prescriptions. The majority of the study population was quite young, with a mean age of 13.5 years [SD = 12.6 - 14.5]. Children under the age of 10 make up 58% of the study population. There was no significant age difference between normal and AS profiles ($p = 0.997$). Age differed significantly between the SS profile and the normal profile ($p < 0.05$). Emergencies and surgeries were more likely to have SS patients (Table 2).

3.2.2. Blood Culture Positivity Rate

Of 19,090 vials examined in this current study, 19.6% developed a positive blood culture. The normal and AS profiles have a similar positivity rate with 19.6% and 19.1% positive vials, respectively. The SC profile had the lowest positivity rate at 11.1%, while the highest values were in the SS with 24.3% positivity (Table 2).

3.2.3. Blood Culture Microorganism Distribution at a Family Level

The most commonly isolated bacteria were Staphylococci (41.1%), Enterobacteriaceae (36.7%), Bacillaceae (10.2%) unfermented (6.30%), Streptococci (5.01%) and a small proportion of yeast (0.75%). There is no significant difference in bacterial spectrum between the SS profile and the normal profile of subjects ($p = 0.104$) (Table 3).

3.2.4. Blood Culture Microorganism Distribution at a Species Level

Coagulase-negative staphylococci accounted for 32%, 24%, and 40% of species

Table 1. Hemoglobin profile and gender of study population.

	normal (N = 1025)	type AS (N = 283)	type SC (N = 7)	type SS (N = 104)	p. overall
Gender:					0.732
Female	38.9% [35.9%; 42.0%]	38.5% [32.8%; 44.5%]	42.9% [9.90%; 81.6%]	44.2% [34.5%; 54.3%]	
Male	61.1% [58.0%; 64.1%]	61.5% [55.5%; 67.2%]	57.1% [18.4%; 90.1%]	55.8% [45.7%; 65.5%]	

Table 2. Blood culture flask origin and positivity.

	[ALL] N = 19,090	normal N = 18,042	type AS N = 677	type SC N = 9	type SS N = 362	p. overall
Origine, N (%):						.
surgery	2.51% [2.29%; 2.74%]	2.61% [2.38%; 2.85%]	1.19% [0.51%; 2.33%]	0.00% [0.00%; 33.6%]	0.00% [0.00%; 1.02%]	
external	5.28% [4.97%; 5.61%]	3.95% [3.67%; 4.25%]	22.7% [19.6%; 26.1%]	44.4% [13.7%; 78.8%]	38.1% [33.0%; 43.3%]	
medicine	14.9% [14.4%; 15.4%]	15.2% [14.7%; 15.8%]	11.1% [8.85%; 13.7%]	11.1% [0.28%; 48.2%]	3.61% [1.94%; 6.10%]	
pediatrics	69.7% [69.0%; 70.3%]	70.3% [69.6%; 71.0%]	61.3% [57.5%; 65.0%]	33.3% [7.49%; 70.1%]	53.6% [48.3%; 58.9%]	
urgency	7.70% [7.32%; 8.08%]	7.90% [7.51%; 8.31%]	3.71% [2.41%; 5.43%]	11.1% [0.28%; 48.2%]	4.72% [2.77%; 7.45%]	
culture, N (%):						**0.139**
positive	19.6% [19.1%; 20.2%]	19.6% [19.0%; 20.1%]	19.1% [16.2%; 22.2%]	11.1% [0.28%; 48.2%]	24.3% [20.0%; 29.1%]	
sterile	80.4% [79.8%; 80.9%]	80.4% [79.9%; 81.0%]	80.9% [77.8%; 83.8%]	88.9% [51.8%; 99.7%]	75.7% [70.9%; 80.0%]	
Age, Mean (SD)	13.7 [13.3; 14.0]	13.8 [13.5; 14.2]	12.5 [11.2; 13.8]	13.8 [4.50; 23.1]	8.51 [7.59; 9.44]	<0.001
Age category, N (%):						.
<01	54.1% [53.4%; 54.8%]	56.7% [56.0%; 57.4%]	13.3% [10.8%; 16.1%]	0.00% [0.00%; 33.6%]	1.93% [0.78%; 3.94%]	
01 - 05	8.73% [8.33%; 9.14%]	7.33% [6.96%; 7.72%]	30.6% [27.1%; 34.2%]	11.1% [0.28%; 48.2%]	37.3% [32.3%; 42.5%]	
05 - 10	6.50% [6.15%; 6.85%]	5.49% [5.16%; 5.84%]	21.3% [18.2%; 24.5%]	55.6% [21.2%; 86.3%]	27.6% [23.1%; 32.5%]	
10 - 20	7.27% [6.91%; 7.65%]	6.58% [6.22%; 6.95%]	16.0% [13.3%; 18.9%]	0.00% [0.00%; 33.6%]	25.7% [21.3%; 30.5%]	
20 - 25	2.50% [2.29%; 2.74%]	2.46% [2.24%; 2.70%]	2.81% [1.70%; 4.35%]	11.1% [0.28%; 48.2%]	3.87% [2.13%; 6.40%]	
25 - 30	2.23% [2.02%; 2.45%]	2.23% [2.02%; 2.46%]	2.66% [1.58%; 4.17%]	0.00% [0.00%; 33.6%]	1.10% [0.30%; 2.80%]	
30 - 35	2.22% [2.02%; 2.44%]	2.30% [2.09%; 2.53%]	0.59% [0.16%; 1.51%]	22.2% [2.81%; 60.0%]	0.83% [0.17%; 2.40%]	
35 - 40	2.00% [1.80%; 2.20%]	2.00% [1.80%; 2.22%]	2.66% [1.58%; 4.17%]	0.00% [0.00%; 33.6%]	0.55% [0.07%; 1.98%]	
40 - 45	1.62% [1.45%; 1.81%]	1.62% [1.44%; 1.82%]	2.22% [1.25%; 3.63%]	0.00% [0.00%; 33.6%]	0.55% [0.07%; 1.98%]	
45 - 50	1.64% [1.46%; 1.83%]	1.68% [1.50%; 1.88%]	1.33% [0.61%; 2.51%]	0.00% [0.00%; 33.6%]	0.00% [0.00%; 1.01%]	
50+	11.2% [10.7%; 11.6%]	11.6% [11.1%; 12.0%]	6.65% [4.89%; 8.79%]	0.00% [0.00%; 33.6%]	0.55% [0.07%; 1.98%]	

Table 3. Microorganism distribution at family level.

	[ALL] N = 19,090 Positive (19.6%)	normal N = 18,042 Positive (19.6%)	type AS N = 677 Positive (19.1%)	type SC N = 9 Positive (11.1%)	type SS N = 362 Positive (24.3%)	p. overall
Bacterium family, N (%):						.
Bacillaceae	10.2% [9.20%; 11.2%]	9.92% [8.95%; 11.0%]	10.1% [5.48%; 16.6%]	0.00% [0.00%; 97.5%]	25.9% [15.0%; 39.7%]	
Enterobacteriaceae	36.7% [35.1%; 38.3%]	37.2% [35.6%; 38.8%]	31.0% [23.2%; 39.7%]	0.00% [0.00%; 97.5%]	18.5% [9.25%; 31.4%]	
Yeast	0.75% [0.50%; 1.09%]	0.51% [0.30%; 0.81%]	7.75% [3.78%; 13.8%]	0.00% [0.00%; 97.5%]	0.00% [0.00%; 6.60%]	
unfermented	6.30% [5.54%; 7.13%]	5.98% [5.22%; 6.81%]	14.0% [8.48%; 21.2%]	100% [2.50%; 100%]	7.41% [2.06%; 17.9%]	
Staphylococci	41.1% [39.5%; 42.7%]	41.3% [39.7%; 42.9%]	34.1% [26.0%; 43.0%]	0.00% [0.00%; 97.5%]	44.4% [30.9%; 58.6%]	
Streptococci	5.01% [4.33%; 5.76%]	5.10% [4.40%; 5.88%]	3.10% [0.85%; 7.75%]	0.00% [0.00%; 97.5%]	3.70% [0.45%; 12.7%]	

isolated in the normal AS and SS profiles, respectively. Coagulase-negative staphylococci were the most frequently isolated germs in SS. Group E streptococci and sp-tagged streptococci each account for less than 2% of the isolated organisms in SS. Pneumococci were not found. *Bacillus* accounts for 25% of isolates in SS subjects compared to 9% in normal and AS subjects, respectively. *Pseudomonas aeruginosa* and *Burkholderia cepacia* then account for 10% of the isolates in the SS profile subjects as non-fermenters.

About 13% is found in subjects with AS profile, while in normal subjects and SC the frequency of *Pseudomonas aeruginosa* and *B. cepacia* does not exceed 5%. *Klebsiella pneumoniae* and *E. coli* are the main isolated Enterobacteriaceae, in normal (19% and 7%) and AS (11% and 8%) profiles, respectively. *E. coli*, *P. mirabilis*, and *Serratia marcescens* appear to be the most important enteric bacteria in SS individuals, accounting for 7%, 3.5%, and 3.5%, respectively. Salmonella was observed in less than 2% of cases, respectively, only in normal and SA-type subjects (Table 4, Figure 2).

4. Discussion

4.1. Bacteremia Occurrence in Sickle Cell Hemoglobinopathy Subjects

4.1.1. Higher Bacteremia Rate in Low-Income Countries

The aim of our study was to determine the positive value of blood culture vials in sickle cell patients compared to normal people. Second, compare the spectrum of bacteria in SCD patients with normal individuals. Bacteremia is quite common in people with sickle cell disease, and in some studies, bacteremia can account for 10% - 32% of the causes of fever [16]. A total of 3741 blood culture

Table 4. Microorganism frequency at the species level.

	normal (Freq)	typeAS (Freq)	type SC (Freq)	type SS (Freq)
Achromobacter sp.	0.0005	0.0000	0.5012	0.0000
Acinetobacter sp.	0.0257	0.0152	0.0000	0.0175
Aeromonas hydrophila	0.0016	0.0000	0.0000	0.0000
Aeromonas sp.	0.0005	0.0000	0.0000	0.0000
Bacillus sp.	0.0987	0.0994	0.0000	0.2462
Burkholderia cepacia	0.0028	0.0152	0.5012	0.0527
Candida albicans	0.0042	0.0459	0.0000	0.0000
Candida sp.	0.0008	0.0306	0.0000	0.0000
Citrobacter amalonaticus	0.0011	0.0000	0.0000	0.0000
Citrobacter farmeri	0.0002	0.0000	0.0000	0.0000
Citrobacter freundi	0.0002	0.0000	0.0000	0.0175
Citrobacter koseri	0.0045	0.0000	0.0000	0.0000
Citrobacter sp.	0.0000	0.0076	0.0000	0.0000
Corynebacterium sp.	0.0050	0.0000	0.0000	0.0000
E. coli	0.0711	0.0841	0.0000	0.0703
enterobacter aerogens	0.0319	0.0535	0.0000	0.0000
enterobacter cloacae	0.0322	0.0152	0.0000	0.0000
Enterobacter sp.	0.0101	0.0000	0.0000	0.0000
Enterococcus faecium	0.0030	0.0000	0.0000	0.0000
Enterococcus sp. coli	0.0047	0.0076	0.0000	0.0000
Klebsiella oxytoca	0.0028	0.0000	0.0000	0.0000
Klebsiella ozaenae	0.0002	0.0000	0.0000	0.0000
Klebsiella pneumoniae	0.1896	0.1070	0.0000	0.0175
Morganella morganii	0.0019	0.0000	0.0000	0.0000
Proteus *mirabilis*	0.0005	0.0000	0.0000	0.0351
Pseudomonas aeruginosa	0.0310	0.1224	0.0000	0.0527
Pseudomonas stutzeri	0.0019	0.0076	0.0000	0.0000
Salmonella enteritidis	0.0011	0.0000	0.0000	0.0000
Salmonella paratyphi A	0.0053	0.0076	0.0000	0.0000
Salmonella sp.	0.0112	0.0152	0.0000	0.0000
Serratia marcescens	0.0028	0.0076	0.0000	0.0351
Serratia odorifera	0.0002	0.0000	0.0000	0.0000
Serratia sp.	0.0002	0.0000	0.0000	0.0000

Continued

Staphylococcus aureus	0.0855	0.0918	0.0000	0.0175
Staphylococcus coagulase negative	0.3256	0.2448	0.0000	0.4044
Streptococcus pneumoniae	0.0028	0.0000	0.0000	0.0000
Streptococcus sp.	0.0008	0.0000	0.0000	0.0175
Streptocoques du groupe A	0.0016	0.0000	0.0000	0.0000
Streptocoques du groupe B	0.0137	0.0000	0.0000	0.0000
Streptocoques du groupe C	0.0002	0.0000	0.0000	0.0000
Streptocoques du groupe D	0.0039	0.0000	0.0000	0.0000
Streptocoques du groupe E	0.0171	0.0230	0.0000	0.0175
Streptocoques du groupe G	0.0011	0.0000	0.0000	0.0000

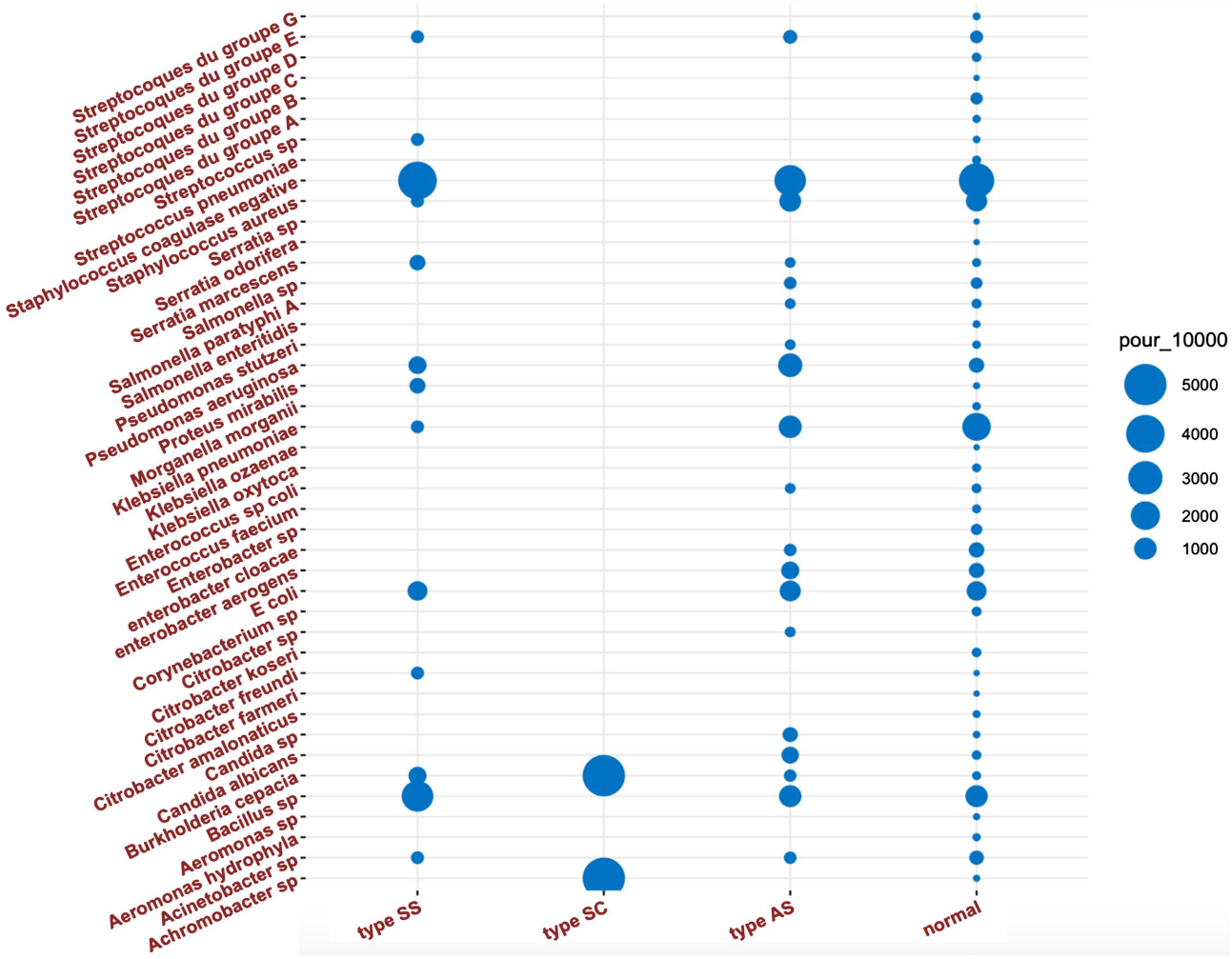

Figure 2. Microorganism frequency distribution at a species level (×10000 scale).

vials showed positive culture in our study on a total of 19,090 vials analyzed. Blood cultures were most frequently positive in homozygotes with a frequency of 24.3% compared to 19.6% in normal profile. Several studies in Africa have

shown the higher frequency of 14% to 32% of bacteremia in patients with sickle cell disease. In Benin, 32.5% of febrile drepanocytes showed bacteremia and similar results of 32.2% were found in Nigeria in Ibadan [15] [16]. A similar study found a slightly lower yield in Saudi Arabia, which was 20.8% or 3546 positive vials from the 17,053 blood cultures tested [17]. In developed countries such as Canada [17], infections are much less common, at only 1.3% among the 692 emergency patients admitted for bacteremia. Similar results were observed in the USA by Bansil [18] and by Morissey [19]. Overall, bacterial infections appear to be less common in developed countries, the USA [18], London [19], and Canada than in sub-Saharan Africa [20]. This disparity could be partly related to better living conditions and better prophylaxis, as well as greater vaccine efficacy [14] [15].

4.1.2. High Rate of Negative Coagulase Staphylococci and *Bacillus*

However, it should be noted that 24.6% and 40.4% of isolates in homozygotes are coagulase negative *Staphylococcus* and *Bacillus* species, respectively, which are mostly considered non-pathogenic. According to some authors, coagulase-negative staphylococci can account for up to 80% of the contaminations in their series [20] [21]. A similar study conducted in Bahrain in a cohort with sickle cell disease showed that *Staphylococcus* epidermidis was the most common germ, isolated in 42.86% of cases. Pathogenicity depends on the expression of virulence factors that are unexplorable in resource-constrained settings. For this reason, if only one bottle is positive for negative staph, contamination is considered. After isolation of negative staphylococci twice, the result is considered positive and an antibiotic susceptibility test is initiated. The greater frequency of contamination in homozygous sickle cell disease may be related to more severe symptomatology, often requiring more blood cultures to find pathogens.

4.2. Bacteremia Spectrum

4.2.1. Predominance of Gram-Negative Bacteremia

Since the introduction of the pneumococcal vaccine, predicting the bacteria involved in septicemia has become increasingly challenging. In many cases, it lies outside the classic pathogen spectrum of sickle cell infection [21]. Our results show that among the proven pathogens, enterobacteria occupy the first place with 29% and 16% in subjects with AS and SS profiles, respectively. This is followed by non-fermenters with 16% and 12% in the AS and SS profile subjects, respectively. Gram-positive cooci rank third position with 5% and 11% respectively in the SS and AS profile subjects. This distribution is quite distant from the classical distribution of the causative agent of sickle cell anemia, in which gram-positive cocci with pneumococci and staphylococci in the head predominate. We did not find isolates of *Streptococcus pneumoniae* in either AS or SS individuals. The first studies on the pathogen spectrum of bacteremia carried out in Lagos in the 1980s already showed a dominance of gram-negative rods with *Klebsiella* spp. (38%), *E. coli* (23%), *Pseudomonas* spp. (23%) [16] [22]. In 1993, Okuonghae

in Nigeria found in 166 repertory infection episodes in 162 drepanocytes that gram-negative germs predominated, accounting for 70.4% of the isolates. Salmonella and *Klebsiella* were the predominant germs, each with 25.9% of all isolates [15]. Similar results were found for Ibadan, where 59% of isolates were Gram-negative and for *Staphylococcus aureus*, the major Gram-positive cocci [15] [22]. It appears that the etiological agents found in sickle cell patients better reflect the microbial ecology of African countries characterized by a dominance of Gram negatives and *Staphylococcus aureus* [23]. First studies carried out in Fann CHU by GAKi-Zerbo between 1985 and 1987 have already shown that 792 blood culture or 80.16% of the total, were gram-negative bacilli [24]. For some authors, the Gram-positive Gram-negative shift begins in the early 1990s with the advent of the first prophylaxis that altered germ ecology and resistance [25].

4.2.2. Low Pneumococci Prevalence

The effectiveness of pneumococcal prophylaxis in developed countries has been supported by several studies, including those conducted in the United States between 1997-2006 and 1998-2018. These two studies both showed a reduction in pneumococcal infections by more than 90% under the effect of vaccination [26] [27]. In our study *Streptococcus pneumoniae* was not found among blood culture isolates. For Akinyanju of the children's emergency hospital, gram-positive cocci were not only a minority, but no more S pneumoniae was found. This observation has already prompted the author to discuss the suitability of European guidelines based mainly on *Streptococcus pneumoniae* prophylaxis in the Nigerian context [22] [28]. Similar results by Alsaif in the vaccine era between 2005 and 2015 showed an important reduction in severe episodes of infection, affecting less than 10% of the febrile sickle cell population. On the other hand, none of these infections was related to *Streptococcus pneumoniae* [29]. For some authors, this could be the result of almost systematic prophylaxis against infections with penicillin and vaccination results in sickle cell disease subjects. Especially since our study population consisted of subjects who benefited from hemoglobin electrophoresis and thus had made clinical arguments likely to initiate pneumococcal prophylaxis. In fact, severe forms of pneumococcal infections continue to be described in the general population, such as at the Albert Royer Center where 218 cases were recorded between 2008 and 2013. However, meningeal and pulmonary forms remained predominant and only 27/218 had bacteremia. Sickle cell disease accounted for only 2.3% of the total study population, suggesting that pneumococcal bacteremia is rare in Senegalese sickle cell patients [30]. According to some authors, the evolution of the affected sickle cells subject in the malaria endemic zone allows maintaining of a certain spleen activity sufficient to fight pneumococcal infections [31].

For other authors, the fetal hemoglobin of the affected sickle cells would play the same protective role in prophylaxis against microorganisms [32]. For other authors, the abuse of antibiotics in prophylaxis could explain the rarity of pneu-

mococci infections in our populations [11]. It is clear that pneumococcus diagnosis can be affected by sub-optimal growing conditions or a low level of pathogens. Therefore, the new diagnostic techniques such as PCR (Polymerase chain reaction) and NGS (new generation sequencing) often make it possible to catch up on false negative blood culture results [33].

5. Conclusion

The retrospective examination of blood cultures among the sickle cell disease subject at the hospital principal in Dakar revealed a positivity rate of 29.5% of blood cultures. Gram-negative bacteria, especially enteric bacteria, are the most common causes of bacteremia. To achieve consensus on initial probabilistic anti-biotherapy, regular monitoring of bacterial ecology and sensitivity is required. Because of the major differences between North and South in the socio-cultural, environmental, and prophylactic variables that influence the determinism of bacterial ecology, further studies are required.

Declarations

Authors' Contributions

All authors were involved in data collection and the preparation of the final manuscript

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

HBsAg	Hepatitis B Surface Antigen
HPD	Principal Hospital of Dakar
WHO	World Health Organization